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EXAMINER	
DEVI, SARVAMANGALA J N	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,381	ANDERSON ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 19-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 19-31* is/are rejected.

7)☒ Claim(s) *32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Request for Continued Examination

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 C.F.R 1.114. Applicant's submission filed on 05/27/09 has been entered.

Applicant's Amendment

2) Acknowledgment is made of Applicant's amendment filed 05/27/09 in response to the final Office Action mailed 01/27/09.

Status of Claims

3) Claims 1, 2, 4, 5, 21-23, 25, 26, 28-30 and 32 have been amended via the amendment filed 05/27/09.

Claims 1-7 and 19-32 are pending and are under examination.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Withdrawn

6) The rejection of claim 26 and the dependent claims 27-32 made in pages 11 and 12 of the Office Action mailed 01/27/09 under 35 U.S.C. § 112, first paragraph, as containing new matter , is withdrawn in light of Applicants' amendment to claim 26.

7) The rejection of claims 1-3, 5-7 and 19-32 made in pages 4-11 of the Office Action mailed 01/27/09 under 35 U.S.C. § 112, first paragraph, as containing inadequate written description, is withdrawn. A modified rejection is set forth below to address the claims as amended. Applicants' arguments are addressed therein to the extent still applicable.

8) The rejection of claims 5-7 made in pages 12 and 13 of the Office Action mailed 01/27/09 under 35 U.S.C. § 102(b) as being anticipated by Foster *et al.* (WO 2003011899 A2, of record) ('899), is withdrawn in light of Applicants' amendment to the base claim.

Claims Rejections under 35 U.S.C § 101

9) 35 U.S.C. § 101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this cycle.

10) Claims 1, 5 and those dependent therefrom are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1 and 5, as written, do not sufficiently distinguish over 'an amino acid sequence of SEQ ID NO: 1', i.e., a fragment of SEQ ID NO: 1, as it exists naturally in the environment, or on the surface of naturally occurring bacteria. The claims do not particularly point out any non-naturally occurring differences between the claimed product and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980)*. Claims should be amended to indicate the hand of the inventor, e.g., by replacing the limitations 'A polypeptide' and 'An immunogen' in claims 1 and 5 respectively with the limitations --An isolated polypeptide-- and --An isolated immunogen-- respectively, if descriptive support exists in the instant specification for such a limitation. See MPEP 2105.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (Written Description)

11) The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12) Claims 1-3, 5-7, 19-23 and 25-31 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The *Written Description Guidelines* state:

> There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between the structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function.

In *Enzo Biochem. Inc. v. Gen-Probe Inc.*, 323 F3.d 956, 964, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002), the Federal Circuit adopted a portion of the Guidelines proffered by the United States Patent and Trademark Office (USPTO). The written description requirement can be met by describing the claimed subject matter to a person skilled in the art using sufficiently detailed, relevant identifying characteristics such as functional characteristics, and correlating those functional characteristics with a disclosed structure. See *Enzo Biochem v. Gen-Probe,* 323 F.3d 956, 964, 967, 968 (Fed. Cir. 2002). Sufficient description to show possession of a *genus* may be achieved by means of disclosure of a representative number of polypeptides, defined by amino acid sequences falling within the scope of the genus, or recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. Possession may *not* be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. See *University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895.

Instant claims, as amended, are not limited to an isolated or purified polypeptide consisting of the amino acid sequence of SEQ ID NO: 1 that provides protective immunity against COL strain of *S. aureus.* Instead, the amended claims are drawn to a *vast genus* of isolated and non-isolated polypeptide immunogens consisting of 'an amino acid sequence of SEQ ID NO: 1', or polypeptide immunogen variants differing in structure from SEQ ID NO: 1 by up to 15, 10, 5 or 1 amino acid alterations, or polypeptide immunogen variants that are 1% non-identical to SEQ ID NO: 1. The limitation 'an amino acid sequence of SEQ ID NO: 1' encompasses innumerable fragments of SEQ ID NO: 1. These fragments and the polypeptide variants having as many as up to 15 amino acid alterations from any region within SEQ ID NO: 1, or having 1% non-identity to SEQ ID NO: 1 are *required* to have the ability to provide protective immunity against any *S. aureus*. The polypeptide immunogen claimed in claims 1-7 and 26 is not required to be purified and/or isolated. The limitation 'patient' in claim 6 encompasses an infant patient, neonate patient, an immunocompromised patient such as a cancer patient, or AIDS patient. The limitation 'amino acid alterations' in the claims, encompasses amino acid substitutions, insertions, additions, and amino

acid deletions. The recited 'amino acid alterations' encompass unidentified or unspecified alterations within SEQ ID NO: 1 at any position of the claimed polypeptide immunogen. The protective immunity induced in humans or animals against any strain of *S. aureus* including non-COL *S. aureus* is not excluded from the scope of the claims. The limitation '*S. aureus*' encompasses homologous or heterologous strains of *S. aureus*, coagulase-positive and coagulase-negative *S. aureus*; multiple drug-resistant and methicillin-resistant strains of *S. aureus* (MRSA), various phage types of *S. aureus*, enterotoxigenic and non-enterotoxigenic *S. aureus,* various other serotypes including non-typeable *S. aureus,* or various capsular types of *S. aureus*. For instance, von Eiff *et al*. (*Diagn. Microbiol. Infect. Dis*. 58: 297-302, 2007, of record) teach the prevalence of clinical isolates of *S. aureus* as various *spa* serotypes and capsular serotypes. See abstract of von Eiff *et al*. von Eiff *et al*. characterize *S. aureus* to be one of the most 'feared' microorganisms because of its ability to cause serious and fatal infections.

A review of the instant application indicates that Applicants have not shown possession of a representative number of altered polypeptide or polypeptide immunogen species having the recited number of amino acid alterations within SEQ ID NO: 1, or the fragments species of SEQ ID NO: 1, wherein the species provide protective immunity against any of the above-exemplified *Staphylococcus aureus*. Applicants submit that the data provided for SEQ ID NO: 3, a His-tagged SEQ ID NO: 1, illustrates that a polypeptide of SEQ ID NO: 1 is able to reproducibly provide for some protective immunity. Applicants contend that Figures 7A and 7B illustrate that more mice survive when immunized with a polypeptide vaccine (SEQ ID NO: 3) than with the adjuvant. Applicants argue that the ability of SEQ ID NO: 3 to provide for protective immunity reasonably conveys to those skilled in the art that Applicants were in possession of polypeptides that have a substantially similar sequence to SEQ ID NO: 1 and provide protective immunity against *S. aureus*. Applicants assert that the reasonable conveyance is provided by the high degree of structural relationship between 'the SEQ ID NO: 1 related polypeptides' recited in the claims. Applicants state that polypeptides differing from SEQ ID NO: 1 by up to 15 amino acids have at least about a 94% degree of sequence identity to SEQ ID NO: 1, the 94% identity being calculated as (260-15)/260 x 100. Applicants further contend that the expectation that a particular sequence 'based on SEQ ID NO: 1' would provide protective immunity increases as the relationship to SEQ ID NO: 1 increases. Applicants allege that the rejection fails to indicate why the overall structural

relationship recited in the claims does not reasonably correlate with the indicated function. Applicants further allege that the rejection does not indicate why in the absence of providing a particular epitope important protection, the skilled artisan making changes would expect a significant number of polypeptides covered by the claims not to provide protective immunity. Applicants argue that the possibility that some alterations would prevent the described polypeptide from providing protective immunity does not take away from the 'overall expectation' of one skilled in the art with respect to polypeptides having a high degree of structural relationship to the polypeptide of SEQ ID NO: 1. Applicants cite case law and submit that the described high degree of structural relationship to SEQ ID NO: 1 provides more than a mere wish for obtaining a compound able to provide protective immunity. Applicants conclude that it provides an expectation that because of the similarity in structure of other polypeptides provided in the claims to SEQ ID NO: 1, the other polypeptide would have a similar function.

Applicants' arguments have been fully considered, but are not persuasive. It is well known in the art that, of a myriad of polypeptides that may be produced by a bacterial or microbial pathogen, not all polypeptides elicit a pathogen-specific immune response that is protective against the pathogen. The art of protective immunogens or vaccines recognizes the unpredictability associated with whether or not an antigen or immunogenic component derived from a microbial pathogen is immunoprotective. For instance, Ellis RW (*Vaccines*, (Eds) Plotkin *et al.*, W.B. Saunders Company, Philadelphia, Chapter 29, 568-575, 1988, see page 571, second full paragraph) reflected this problem in the teaching that the key to the problem of vaccine development "is the identification of that protein component of a ..... microbial pathogen that itself can elicit the production of protective antibodies ..... and thus protect the host against attack by the pathogen". This is particularly important in the instant application because Applicants' SEQ ID NO: 1 is **not** a native polypeptide produced by one or more strains of *S. aureus.* Instead, SEQ ID NO: 1 is a considerably structurally-altered transferring binding protein of *S. aureus.* For example, see third full paragraph from below on page 5 of the instant specification which is reproduced below [Emphasis added]:

> 'SEQ ID NO: 1 was produced based on a full length transferring binding protein by **modifying** the encoding nucleic acid **to remove** the amino signal sequence, **to remove** a carboxyl hydrophobic region, **to add** an amino terminus methionine, and **to add** a restriction site to the amino terminus. The removed hydrophobic region followed a LPXTG motif. The addition of the amino terminus restriction site resulted in a **Serine to Glycine substitution**.'

No one or more conformational or non-conformational, contiguous or discontiguous epitopes within SEQ ID NO: 1, let alone its 1% non-identical variants, up to 15 amino acids-altered variants, and its fragments, have been identified or adequately described in the instant application or in the state of the art at the time of the invention, which one or more epitopes provide protective immunity against homologous or heterologous *S. aureus*. Contrary to the Applicants' argument, SEQ ID NO: 3 is not representative of the full scope of the claimed altered variant species of SEQ ID NO: 1 or the fragment species of SEQ ID NO: 1, because SEQ ID NO: 3 does not contain up to 15 amino acid alterations *within* SEQ ID NO: 1 and does not represent a fragment of SEQ ID NO: 1 that contains one or more protective epitopes therein which epitopes provide protective immunity against homologous or heterologous strains of *S. aureus*, coagulase-positive and coagulase-negative *S. aureus*; multiple drug-resistant and methicillin-resistant strains of *S. aureus* (MRSA), various phage types of *S. aureus*, enterotoxigenic and non-enterotoxigenic *S. aureus,* various other serotypes including non-typeable *S. aureus,* or various capsular types of *S. aureus*. Instead, SEQ ID NO: 3 contains all of SEQ ID NO: 1 and a His-tag at the amino terminus of SEQ ID NO: 1. Clearly, Applicants have not shown that a representative number of variant species and fragment species of the considerably altered SEQ ID NO: 1 as claimed, are indeed produced by COL or non-COL strains of *S. aureus* and/or would automatically provide protective immunity against COL or non-COL strains of *S. aureus*. The precise structure of a representative number of variant species and fragment species of SEQ ID NO: 1 has not been correlated with the requisite function, i.e., induction of protective immunity against any strain of *S. aureus*. This is important because the art reflects unpredictability as to which amino acids in a specific protein can be varied, i.e., replaced or added, without adversely affecting the functional properties of that specific protein. While it is known in the art that variation in one or more amino acids is possible in a given protein, the exact position within its amino acid sequence where replacements or variations can be made, with a reasonable expectation of success of retaining the protein's functional integrity, is not certain. A random replacement affecting the epitopic amino acid positions that are critical, for example, to the three-dimensional conformational structure and specific binding property of the protein, would result in a polypeptide that may be non-functional (i.e., non-immunogenic) or not optimally immunogenic

or protective as a vaccine candidate, because such positions tolerate no or little modifications. As set forth previously, Houghten *et al.* (New Approaches to Immunization, *Vaccines86*, Cold Spring Harbor Laboratory, p. 21-25, 1986) teach the criticality of individual amino acid residues and their positions in peptide antigen-antibody interactions. Houghten *et al.* state (see page 24) [Emphasis added]:

> One could expect point mutations in the protein antigen to cause varying degrees of loss of protection, depending on the relative importance of the binding interaction of the altered residue. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool.

Thus, the art reflects that variations in critical residues at specific positions in an amino acid sequence could result in a polypeptide which may induce an antibody that may not recognize or bind to the native polypeptide of a microorganism. In the instant case, this is important because one of the purposes of the instant invention is to produce a polypeptide or immunogen variant of SEQ ID NO: 1 and fragments of SEQ ID NO: 1 having the capacity to provide protective immunity against any *S. aureus*. The instant disclosure lacks adequate description on the precise position(s), and nature of amino acid replacements or variations that can be made within SEQ ID NO: 1 such that the claimed variants and fragments are produced that have the recited requisite function.

It is well recognized among those of skill in the art that assigning functional activities for any particular protein or a family of proteins based upon sequence homology is inaccurate, partly because of the multifunctional nature of proteins. See abstract and page 34 of Skolnick *et al.* (*Trends in Biotechnology* 18: 34-39, 2000). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein. See abstract and Box 2 of Skolnick *et al.* In the instant application, the recited genus of polypeptide variants having 1% non-identity to SEQ ID NO:1, having up to 15 amino acid alterations within SEQ ID NO: 1, and fragments of SEQ ID NO:1 have been assigned the functional capacity of providing protective immunity against any *S. aureus*. However, there is no showing of a definitive correlation or nexus between the precise structure of a representative number of the various variants and fragments of SEQ ID NO: 1 and the induction of protective immunity against any *S. aureus*,

without which one of skill in the art would not be able to avoid alterations, deletions, or substitutions in those regions, or among amino acid residues within SEQ ID NO: 1, while producing species of the genus of polypeptide immunogen variants having up to 15 amino acid alterations, 1% non-identity to SEQ ID NO: 1, and fragments of SEQ ID NO: 1 having the required function.

The written description for the novel aspects of the invention has to come either from Applicants' disclosure or from the state of the art at the time of the invention. The state of the art at the time of the invention appears to be silent on the protective capacity of sai-1 polypeptide referred to as SfbA by Taylor *et al. Mol. Microbiol.* 43: 1603-1614, 2002 (of record). Applicants have previously submitted that Taylor *et al.* fail to indicate that StbA can be successfully targeted to produce a protective immune response. Taylor's alleged teaching that the *stbA* coding region is well conserved among different *S. aureus* strains does not provide adequate written description for the instantly claimed vast genus of isolated polypeptides consisting of an amino acid sequence with up to 1, 5, 10 or 15 amino acid alterations in SEQ ID NO: 1 or 1% non-identity to SEQ ID NO: 1 (i.e., polypeptide variants) and fragments of SEQ ID NO: 1 providing non-conserved protection against *S. aureus*, or conserved protection against different *S. aureus* strains. What are being claimed are not conserved *stbA* polypeptides, but altered polypeptides and fragments of SEQ ID NO: 1 as claimed that are required to provide protective immunity against *S. aureus.* Furthermore, a review of the instant specification indicates that the animal model that is used in the instant specification to demonstrate protection is limited to a murine model that uses challenge infection with an unspecified strain of *Staphylococcus aureus* followed by monitoring of the survival of immunized and control mice. The survival results from two *in vivo* experiments are depicted in Figure 7. Mice were immunized with three injections of three 20 microgram doses of His-tagged SEQ ID NO: 1 mixed with 450 micrograms of aluminum hydroxyphosphate (AHP) adjuvant. The AHP-injected mice served as controls. The immunized and control mice were challenge-infected 35 days post-immunization with 8×10^8 CFU of *S. aureus*. Whether or not the strain of *S. aureus* used in the challenge infection was a homologous *S. aureus* strain from which the polypeptide was obtained, or a heterologous strain, a virulent strain, or a non-virulent commensal strain, coagulase-positive and coagulase-negative *S. aureus*; multiple drug-resistant or methicillin-resistant strain of *S. aureus* (MRSA), an enterotoxigenic *S. aureus*, a specific capsular

type or phage type of *S. aureus*, or a non-typeable *S. aureus,* is not disclosed. This is particularly important because no significant protection could be demonstrated in immunized mice compared to AHP-injected control mice. Figure 7A demonstrates that three doses of the polypeptide of SEQ ID NO: 3 (i.e., His-tagged SEQ ID NO: 1) administered to mice in aluminum hydroxyphosphate adjuvant (AHP) showed a poor or insignificant survival at day 10 post-challenge compared to the AHP adjuvant alone administered to control mice against intravenous challenge with an unspecified strain of *S. aureus*. Figure 7B illustrates that a polypeptide referred to merely as a 'vaccine' showed less than 60% survival compared to about 45% survival seen in mice immunized with the AHP adjuvant alone. Clearly, even with the single SEQ ID NO: 1 polypeptide species that is His-tagged, the protection conferred by the species does not appear to be significant compared to that seen in mice immunized with AHP alone. No other isolated polypeptide species having 1, or up to 5, 10 or 20 amino acid alterations in SEQ ID NO: 1, a polypeptide having 1% non-identity to SEQ ID NO: 1, or fragments of SEQ ID NO: 1, with or without containing additional moieties at the amino or the carboxyl terminus of the polypeptide, and concurrently having the ability to provide protective immunity against one or more homologous or heterologous strains of *S. aureus,* were in Applicants' possession at the time of the invention. Clearly, as of the filing date sought, Applicants were not in possession full scope '*of the invention*'. Even if one considered the percent survival of immunized mice obtained in the instant specification as representing acceptable/significant protection against one strain of *S. aureus,* the description of one single species of a polypeptide immunogen consisting of a recombinant His-tagged SEQ ID NO: 1 does not provide adequate written description for the whole genus of polypeptide immunogen variant species having up to 15 amino acid alterations in SEQ ID NO: 1, or having 1% non-identity to SEQ ID NO: 1, or the fragments species of SEQ ID NO: 1. The description of a single polypeptide immunogen species within the recited genus may not be sufficient to support the patentability of the genus under 35 U.S.C § 112, first paragraph. See *University of California v. Eli Lilly & Co.*, 119 F.3d 15559, 1567, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997). The specification does not disclose the precise structure of a representative number of altered polypeptide immunogen species in which an amino acid sequence consisting essentially of, or consisting of SEQ ID NO: 1 is altered to contain up to 15 amino acid alterations, or that are 1% non-identical to said SEQ ID NO: 1, or fragments of SEQ ID NO: 1, wherein the

polypeptide variants and fragments have the recited requisite protection function. The instant specification does not disclose which up to 15 amino acid residues within SEQ ID NO: 1, or which 1% of amino acid residues within SEQ ID NO: 1, should be altered in order to maintain the required biological function, i.e., the capacity to provide the broadly recited protective immunity against *S. aureus*. It should be noted that written description requires more than a mere statement that something is a part of the invention. Applicants have not described what domains, contiguous or discontiguous antigenic determinants, or conformational or non-conformational epitopes of the recited altered polypeptide immunogen are correlated with the required capacity to provide protective immunity against homologous or heterologous *S. aureus*.

With respect to the written description requirement, while 'examples explicitly covering the full scope of the claim language' typically will not be required, a sufficient number of representative species must be included 'to demonstrate that the patentee possesses the full scope of the [claimed] invention'. *Lizardtech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345, 76 USPQ2d 1724, 1732 (Fed. Cir. 2005). In the instant case, Applicants' specification does not contain a written description sufficient to show they had possession of the full scope of their claimed invention at the time the application was filed. The specification does not disclose a correlation between the function (i.e., capacity to provide protective immunity against *S. aureus*) and the precise structure, or conformational or non-conformational epitope(s) responsible for providing such protective immunity such that a skilled artisan would have known what alterations including deletions, substitutions, additions, or other variations could be made of the large number of alterations currently encompassed within the scope of the instant claims without losing the protective function. Clearly, Applicants did not describe the invention of the instant claims sufficiently to show that they had possession of the recited genus of altered polypeptide immunogens claimed. See e.g., *Noelle v. Lederman*, 355 F.3d 1343, 1348, 69 USPQ2d 1508, 1513 (Fed. Cir. 2004) ('invention is, for purposes of the written description inquiry, *whatever is now claimed*'). Applicants should note that written description requires more than a mere statement that something is a part of the invention and a reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

As known in the art of immunology, an epitope or antigenic determinant can be linear, or conformational or discontinuous, and it interacts with its corresponding antibody based on the three dimensional structure of both molecules and the fit between the molecules. See page 46 of Cruse *et al*., *Illustrated Dictionary of Immunology*, 2nd Edn., CRC Press, 2003, of record. The specification does not adequately describe or identify the *S. aureus*-specific, or *S. aureus* serotype-specific, non-serotype-specific or *S. aureus* strain-specific linear or conformational protective epitopes within SEQ ID NO: 1 or within an amino acid sequence with up to 15 amino acid alterations within SEQ ID NO: 1, or within an amino acid sequence that is 1% non-identical to SEQ ID NO: 1, or within fragments of SEQ ID NO: 1. This description is important because for an altered polypeptide or a polypeptide fragment to be protective, it has to minimally bind immunospecifically with a native polypeptide-specific protective antibody. A change of even a single amino acid residue is known to alter the folding of a polypeptide such that the antibody-binding region no longer recognizes the polypeptide. See right column on page 33 of Colman PM. *Research Immunol*. 145: 33-36, 1994, of record. It is recognized in the art that even a very conservative substitution may abolish binding. See first full paragraph on page 35 of Colman. Colman further taught that binding interactions could be considered less tolerant because the changes involved occur in what might be called the active site. See third full paragraph on page 35 of Colman. There is no disclosure as to which amino acids at which positions can be substituted such that one can obtain the altered polypeptide that has the required immunological specificity to be protective against any *S. aureus*. This is important because the claimed altered polypeptide species or the fragment species have specific biological properties dictated by the structure of the polypeptide and the corresponding structure of the structural gene sequence which encodes it. There has to be some nexus between the structure of the altered polypeptide sequence and the function of such a polypeptide. However, the function cannot be predicted from the modification or alteration of the structure of the recited polypeptide. Applicants have not shown that up to 15 amino acid alterations within the polypeptide of SEQ ID NO: 1 would automatically predict the production of altered polypeptides having the required functions. The specification fails to teach the structure or precise relevant identifying characteristics of a representative number of such altered polypeptide species sufficient to allow one skilled in the art to determine that inventors had possession of the invention as claimed. Applicants have not described which

domains or regions of the recited polypeptide immunogen variants are correlated with the required capacity to provide such protective immunity. Applicants have not described which of SEQ ID NO: 1's amino acids can be varied such that the polypeptide immunogen variant still maintains the capacity to provide such broad protective immunity. Without a convincing correlation between structure and function, the claims do little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *Ex parte Kubin*, 83 USPQ2d 1410 (Bd. Pat. Appl. & Int. 2007) citing *Eli Lilly*, 119 F.3d at 1568, 43 USPQ at 1406 ('definition by function ….. does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is'). The instant claims are viewed as not meeting the written description provision of 35 U.S.C. § 112, first paragraph. The Office has clearly met the burden of presenting a *prima facie* case lack of adequate written description.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (New Matter)

13) Claims 1-3, 5-7 and 19-31 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Independent claims 1, 5 and 26, as amended, include the limitations: 'consisting of *an* amino acid sequence of SEQ ID NO: 1 or a sequence that differs from SEQ ID NO: 1 by up to 15 amino acid alterations, … wherein said polypeptide immunogen provides protective immunity against *S. aureus*'. The limitation 'an amino acid sequence of SEQ ID NO: 1' encompasses multiple fragment species of SEQ ID NO: 1 or fragment species from any region from within SEQ ID NO: 1 each having the requisite capacity to provide protective immunity against *S. aureus*. Similarly, the limitation 'immunogen consisting of …. a sequence that differs from SEQ ID NO: 1 by up to 15 amino acid alterations' encompasses numerous immunogen species each consisting of a sequence with up to 15 variations, substitutions, insertions, or deletions from within SEQ ID NO: 1 and each having the *requisite* capacity to provide protective immunity as recited. The encompassed fragment species of SEQ ID NO: 1 and the recited sequence species differing from SEQ ID NO: 1 by up to 15 amino acid alterations are both *required* to provide immunity against any strain or isolate of *S. aureus*. Applicants state that the amendment to claim

1 more closely tracts the language provided at second full paragraph on page 7 of the specification. However, this part of the specification does not describe an immunogen or a polypeptide immunogen 'consisting of' any fragment of SEQ ID NO: 1, or of a sequence differing from SEQ ID NO: 1 by up to 15 amino acid alterations, with or without one or more additional moieties, wherein each provides immunity against any strain or isolate of *S. aureus*. Therefore, the above-identified limitations in the amended claim(s) and the current scope of the claim are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the new limitation(s), or alternatively, remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

14) Claim 5 and those dependent therefrom are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 5, as amended currently, includes the limitation: 'wherein said sai-1 region is present on a sequence found in a *S. aureus* sequence'. With this amendment, the recited sai-1 region is *required* to be present 'on' a sequence found 'in' a *S. aureus* sequence having at least 30 contiguous amino acids as provided in SEQ ID NO: 1. Applicants state that support for the amendment can be found on page 3, second paragraph and page 6, fourth paragraph. However, these parts of the specification do not provide descriptive support for a sai-1 region of microbial or non-microbial origin that is present 'on' a sequence found 'in' a *S. aureus* sequence as recited. Therefore, the identified limitation(s) in the claim are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are invited to point to the descriptive support in specific pages and lines of the disclosure, as originally filed, for the limitation identified above, or alternatively, remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

15) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

16) Claims 3-7, 24, 29 and 31 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 3, which depends from claim 1, is indefinite and internally inconsistent because it is improperly broadening in scope in the limitation 'said polypeptide immunogen consists essentially of'. The instant specification at third full paragraph on page 7 defines the term 'consists essentially' as including the presence of additional amino acids in addition to the indicated amino acids and being equivalent to the open claim language 'comprising'. Claim 1 from which claim 3 depends uses the closed claim language 'polypeptide immunogen consisting of'. Therefore, the use of the limitation 'consisting essentially of' which is being equivalent to 'comprising' in the dependent claim 3 renders the claim indefinite.

(b) Analogous rejection and criticism apply to the dependent claims 24 and 31 with regard to the limitation 'said polypeptide immunogen consists essentially of'.

(c) Claim 5 is indefinite and confusing in the limitation: 'sai-1 region is present on a sequence found in a *S. aureus* sequence', because it is unclear whether sai-1 region is a non-peptide or non-protein region that is present 'on' a nucleotide sequence found 'in' a *S. aureus* protein or nucleotide sequence. The structure, nature, size, or origin of 'an sai-1 region' that is present on a sequence as recited is not clear and the metes and bounds of the claim are indeterminate.

(d) Claim 5 is indefinite because it is incorrect in the limitation: 'an sai-1 region' as opposed to the limitation --a sai-1 region--.

(e) Claim 29 is incorrect in the limitation: differs from SEQ ID NO: 1 'by with'.

(f) Claims 4, which depends from claim 3; claims 6 and 7, which depend from claim 5; claims 5 and 7, which depend from claim 5, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C § 102

17) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(e)** the invention was described in-
> **(2)** a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

18) Claims 1, 5-7, 19, 21-23 and 26-30 are rejected under 35 U.S.C. § 102(e)(2) as being anticipated by Granoff *et al.* (US 7,534,444, filed 04/17/01) ('444).

It is noted that the phrase in the amended claim 5 'wherein said sai-1 region is present on a sequence found in a *S. aureus* sequence having at least 30 contiguous amino acids as provided in SEQ ID NO: 1' does not add to the structure of the 'immunogen' claimed therein, since the claimed immunogen consists of element (i) and element (ii) that is 'different from an sai-1 region'. It is further noted that the limitation in claim 5 'an sai-1 region' lacks an origin, size or structure limit.

Granoff *et al.* ('444) disclosed an isolated and purified polypeptide consisting of the amino acid sequence, QTP, and a polypeptide consisting of QTP and an additional region or moiety sequence, FVQ or VHS covalently joined to said QTP sequence at its amino or carboxy terminus respectively. A composition comprising an immunologically effective amount of the same in a pharmaceutically acceptable carrier and an adjuvant is taught. See Figures 4A and 4B; lines 23-61 in column 5; lines 10-13 of column 4; lines 34-40 in column 7; last paragraph in columns 22 and 24; first paragraph in column 23; and paragraph bridging columns 15 and 16. The prior art polypeptide immunogen binds to a specific bactericidal protective antibody and therefore contains a protective epitope. The prior art sequence polypeptide consisting of the QTP sequence constitutes 'an amino acid sequence of SEQ ID NO: 1' since it forms a fragment of the instantly recited SEQ ID NO: 1 that is located at its 210-212 positions. The FVQ region or

moiety present at the amino terminus or the QTP sequence or the VHA region or moiety present at the carboxyl terminus of the QTP sequence is different from an sai-1 region and is expected to facilitate polypeptide stability. The Office's position that the prior art polypeptide is the same as the instantly claimed polypeptide or immunogen is based on the fact that the prior art QTP sequence is structurally identical to 'an amino acid sequence of SEQ ID NO: 1'. The ability to provide protective immunity against *S. aureus* or *S. aureus* COL is viewed as an inherent property inseparable from the prior art sequence and the prior art composition comprising the sequence.

Claims 1, 5-7, 19, 21-23 and 26-30 are anticipated by Granoff *et al.*

Remarks

19) Claims 1-7 and 19-31 stand rejected.

Claim 32 is objected to as being dependent from a rejected claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

20) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

21) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

22) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on

Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Robert Mondesi, can be reached on (571) 272-0956.

/S. Devi/
Primary Examiner
AU 1645

August, 2009